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*Original Article*

## Evaluation of the Appropriate Root Pressure for Maintaining Heartbeat during an Aortic Cross-clamp for Primary Repair of the Aortic Arch in Premature Infants with Associated Cardiac Anomalies

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We developed a new cardiopulmonary bypass (CPB) method to minimize myocardial damage during aortic arch reconstruction. In this method, coronary flow and heartbeat were stabilized by maintaining the aortic root pressure with an adjusted preload of the ventricle during aortic cross-clamping. This study was performed to determine the appropriate root pressure to maintain the heartbeat without causing deterioration of ventricular function. Study 1. Under partial CPB, the ascending aorta was cross-clamped in 6 pigs (group 1). Experimental data at various systolic aortic root pressures was analysed to determine the appropriate root pressure. Study 2. In group 2 (control,  $n=6$ ), the aorta was not clamped, while in group 3 ( $n=6$ ), the aorta was cross-clamped for 60 min and the systolic aortic root pressure was maintained at the pressure determined in study 1. Study 1. The diastolic coronary flow was stabilized at values comparable to that before initiation of CPB ( $6.6 \pm 1.4$  ml/beat) when the systolic aortic root pressure was above 80 mmHg. Intracardiac pressure and the myocardial oxygen consumption ( $MvO_2$ ) seemed to be acceptable when the systolic aortic root pressure was below 100 mmHg. Therefore, 90 mmHg was selected for study 2. Study 2. Perioperative cardiac function did not differ between the groups. We concluded that 90 mmHg was the systolic aortic root pressure appropriate for this method.

**Key words:** aortic cross-clamp, coronary flow, root pressure, cardiopulmonary bypass, arch repair

Primary repair of aortic arch obstructions and associated cardiac anomalies in premature infants is a surgical challenge. It is crucial to the survival of these fragile patients to avoid or minimize myocardial ischemia and total circulatory arrest. In 1990, Sano and Mee introduced an isolated myocar-

dial perfusion technique using an aortic root cannula to reduce myocardial ischemia [1]. In 1996, Ishino and Sano introduced an innominate arterial perfusion technique to perform distal arch anastomosis with continuous cerebral and myocardial perfusion by clamping the arch just distal to the innominate artery [2]. This method, however, requires a short period of cardiac arrest to complete a proximal anastomosis. Lim and his colleagues have reported a combined perfusion technique using a dual arterial cannula: one

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was placed in the innominate artery and the other in the aortic root [3]. By snaring the innominate artery and cross-clamping the ascending aorta, arch repair was performed that retained both continuous cerebral perfusion and a non-working beating heart. The placement of the aortic root cannula, however, can be hazardous, particularly in small infants. To overcome these problems, we have developed a new cardiopulmonary bypass (CPB) method for aortic arch repair in premature babies, wherein the heartbeat is maintained with an aortic cross-clamp during arch repair [4]. In this method, the preload of both ventricles is controlled to maintain coronary forward flow during aortic cross-clamping under partial CPB established between the innominate artery and right atrium. This technique not only enables the arch anastomosis without cessation of brain and myocardial perfusion but also provides the surgeon with excellent exposure of the ascending aorta and entire aortic arch, even in premature infants. However, the condition of the coronary circulation during aortic cross-clamping and the influence of the CPB method on the cardiac function remain unclear. To determine the appropriate systolic aortic root pressure to keep the heart beating without cardiac overload, coronary flow, intracardiac pressure and myocardial  $O_2$  consumption ( $MvO_2$ ) during aortic cross-clamping were herein elucidated at various systolic aortic root pressures. We evaluated the perioperative cardiac function to verify the systolic aortic root pressure. A 60-minute aortic cross-clamp time was selected because the aortic arch could be repaired within this time. The pig was selected as a model because its cardiac physiology resembles that of the human in terms of ventricular performance and coronary distribution [5].

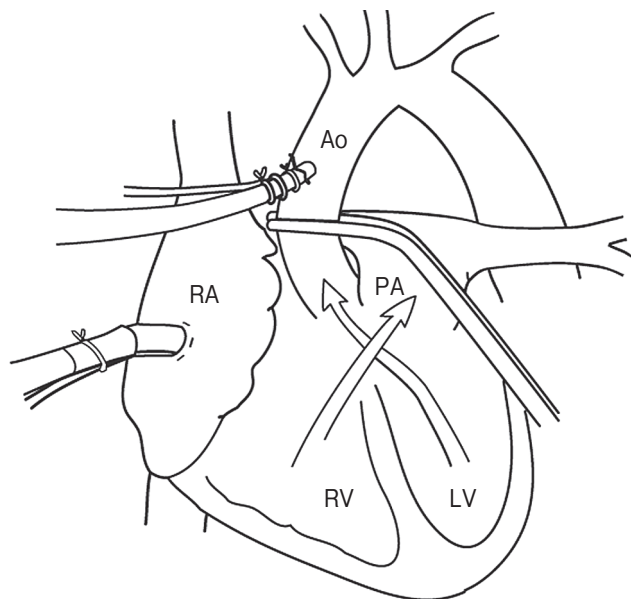
## Materials and Methods

**Pig preparation.** This study was approved by the Animal Research Committee of our institution. The entire process was performed under germ-free conditions.

Eighteen juvenile male and female pigs, weighing  $20 \pm 2$  kg, with normal hearts were used in the experiments. Anaesthesia was induced by intramuscular injection of ketamine (10 mg/kg) and azaperone (4 mg/kg) [6]. After tracheal intubation, the lungs were mechanically ventilated with a fractional inspired

oxygen concentration equal to 1.0 and with a tidal volume of 10 ml/kg. Anaesthesia was maintained with isoflurane (1.2 vol. %). Lactated Ringer's solution was infused at a constant rate of 5 ml/kg/h and the rectal temperature was maintained at 35°C. An arterial line was inserted into the left common carotid artery for continuous measurement of arterial pressure and for collection of samples for arterial blood gas analysis. A central venous line was inserted into the internal jugular vein for continuous measurement of central venous pressure (CVP) and for administration of heparin for anticoagulation. The heart was exposed through a median sternotomy. The animals were heparinized (500 U/kg). A 7-Fr pulmonary artery thermodilution catheter was inserted into the pulmonary artery for cardiac output measurement. A micro-manometer-tip pressure transducer (model SPR543; Millar Instruments, Houston, TX, USA) was introduced into the left ventricle through the apex to measure the left ventricular pressure (LVP). Positive and negative rates of LVP development ( $\pm dp/dt$ ) were obtained from the LVP pulse using an electronic differentiator. A 4-Fr catheter was inserted into the left atrium to measure the left atrial pressure (LAP). Another 4-Fr catheter was inserted into the great cardiac vein for venous blood sampling to measure venous oxygen saturation ( $SvO_2$ ). Coronary flow was measured directly using a 2-mm Transonic flow probe (model No. A2; Transonic Systems Inc., Ithaca, NY, USA) placed on the left anterior descending branch (LAD) and connected to an ultrasonic blood flow meter (model T201; Transonic Systems Inc.). A 24-gauge angiocatheter was also inserted into the aortic root for measurement of the root pressure and sampling of the blood supply to the coronary artery for gas analysis, including arterial oxyhemoglobin saturation ( $SaO_2$ ). The LAD coronary flow, CVP, LAP, LVP, aortic root pressure and electrocardiogram were continuously monitored. All monitoring data were stored using PowerLab software (version 4.1.2; ADInstruments, New South Wales, Australia) for data analysis. Coronary flow was calculated from the integral cross section of the velocity curve.  $MvO_2$  was calculated from the coronary arterio-venous oxygen difference and coronary flow. The azygos and hemiazygos veins, which drain into the superior vena cava and the atrium, respectively, were tied off [7]. Using a roller pump (Cobe Industries, Denver, CO,

USA), normothermic partial CPB was established between the ascending aorta and right atrium. CPB was maintained at a flow of 75 ml/kg/min [8-9]. To normalize the measured LAD flow to 100 g wet tissue,



**Fig. 1** Schema of aortic cross-clamping during partial cardiopulmonary bypass established between the ascending aorta and right atrium. Under this condition, coronary forward flow and heartbeat were dependent on the preload of ventricles. Ao, Aorta; LV, Left ventricle; PA, Pulmonary artery; RA, Right atrium; RV, Right ventricle.

at the end of all procedures, Evans Blue (2.5%) was slowly injected into the LAD at the point where the ultrasonic flow meter was connected, and the total mass perfused by LAD was later determined by weighing the stained tissue [10].

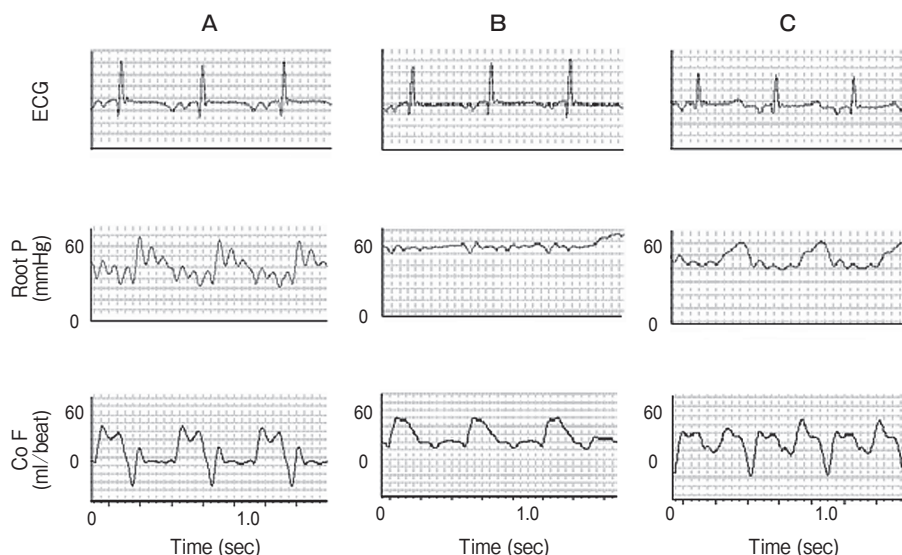
### **Experimental protocols.**

#### **Study 1. Preliminary study**

Under normothermic partial CPB, the ascending aorta was cross-clamped proximal to the aortic root cannula in each of the 6 pigs in group 1 (Fig. 1). By increasing the ventricular preload, the systolic aortic root pressure was elevated in a stepwise fashion from 60 mmHg to 140 mmHg. After 10 min of static state at each systolic aortic root pressure of 60, 80, 100, 120 and 140 mmHg, monitoring data were collected and blood was sampled. These data at each systolic aortic root pressure were compared with the data prior to CPB to determine the appropriate systolic aortic root pressure to keep the heart beating with an acceptable cardiac preload during aortic cross-clamping.

#### **Study 2.**

In the 6 pigs in group 2 (control group), normothermic partial CPB was performed without aortic cross-clamping. In group 3, the ascending aorta was cross-clamped for 60 min under normothermic partial CPB. The systolic aortic root pressure determined in the preliminary study was maintained. After 60 min of aortic cross-clamping, CPB was terminated without



**Fig. 2** Actual tracings (A) before and (B) after the initiation of partial cardiopulmonary bypass and (C) during aortic cross-clamp. Root P, Root pressure; Co F, Coronary flow.

any catecholamine. MvO<sub>2</sub> was calculated at 10 min intervals. The left ventricular ejection fraction on echocardiogram, cardiac output,  $\pm dp/dt$  and troponin T were measured before initiation and 120 min after the termination of CPB for both groups.

**Statistical analyses.** Wilcoxon's test was used for paired samples. A probability of less than 0.05 ( $p < 0.05$ ) was considered statistically significant.

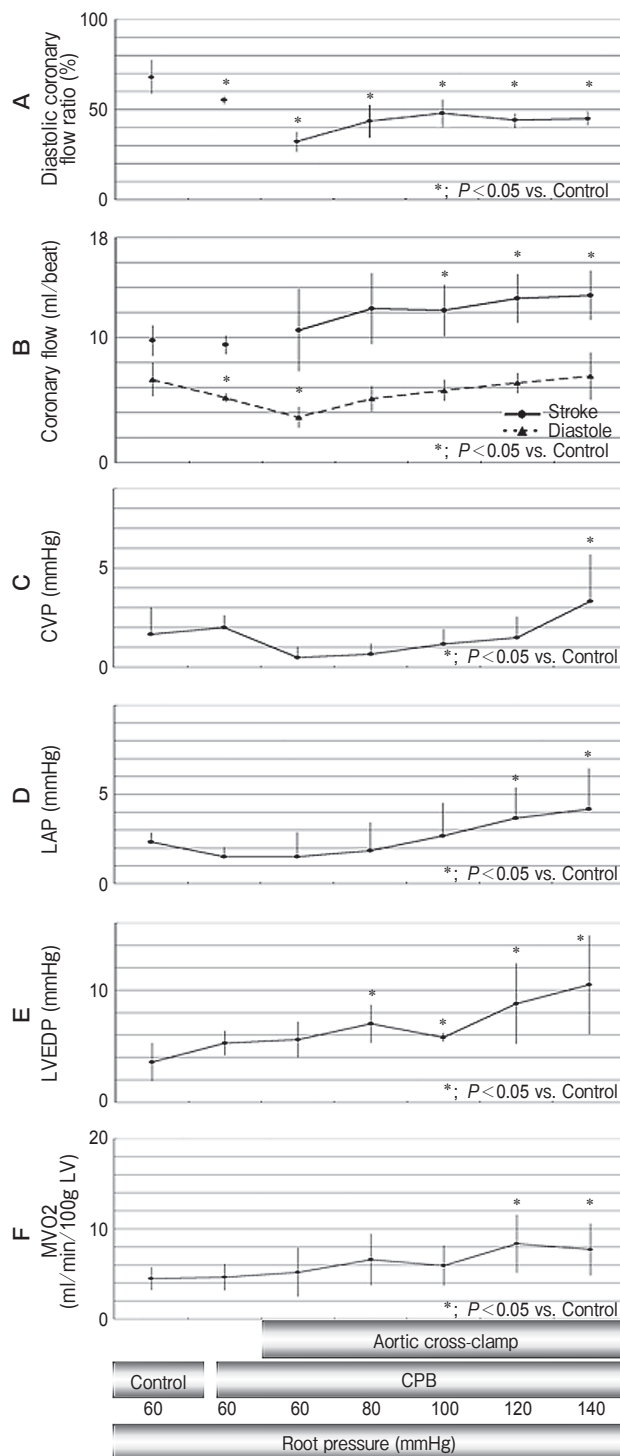
## Results

### Study 1. Preliminary study

Throughout the study, the pigs' heart rates did not change significantly. Coronary flow was dominant during diastole before the initiation of CPB and under the partial CPB; however, it was dominant during systole at every systolic aortic root pressure after the aorta was cross-clamped (Fig. 2, 3A). The diastolic coronary flow ratio during aortic cross-clamping was especially low, at a systolic aortic root pressure of 60 mmHg ( $32 \pm 6\%$ ), and it reached a plateau at 80 mmHg ( $44 \pm 9\%$ ). With the elevation of systolic aortic root pressure, diastolic coronary flow increased. As a result, diastolic coronary flow at the systolic aortic root pressures above 80 mmHg ( $5.1 \pm 1.0$  ml/beat) was equivalent to that before initiation of CPB ( $6.6 \pm 1.3$  ml/beat) (Fig. 3B). CVP, LAP and MvO<sub>2</sub> at the systolic aortic root pressures below 100 mmHg were also equivalent to those before initiation of CPB (Fig. 3C, 3D, 3F). Left ventricular end-diastolic pressure (LVEDP) at 80 and 100 mmHg of systolic aortic root pressures ( $7 \pm 1.7$  mmHg and  $5.8 \pm 0.4$  mmHg) were significantly higher than that before initiation of CPB ( $3.6 \pm 1.7$  mmHg); although low, these pressures were at an acceptable level (Fig. 3E). Based on these results, 90 mmHg of systolic aortic root pressure seemed to be appropriate to keep the heart beating without significant cardiac overload.

### Study 2.

During a 60-minute aortic cross-clamping at 90 mmHg of systolic aortic root pressure, no ST change or bradycardia in any of the 6 pigs in group 3 was observed on an electrocardiogram. MvO<sub>2</sub> increased during the first 30 min and declined during the latter half of the experiment, but there was no significant difference in MvO<sub>2</sub> between groups 2 and 3 throughout the procedure (Fig. 4). Also, there was no significant difference between the 2 groups in left ven-



**Fig. 3** (A) Diastolic coronary flow ratio, (B) Diastolic and stroke coronary flow, (C) CVP, (D) LAP, (E) LVEDP and (F) MvO<sub>2</sub> in study 1. CPB, Cardiopulmonary bypass; CVP, Central venous pressure; LAP, Left atrial pressure; LVEDP, Left ventricular end-diastolic pressure; MvO<sub>2</sub>, Myocardial O<sub>2</sub> consumption.

tricular ejection fraction, cardiac output,  $\pm dp/dt$  and troponin T as measured before initiation and 120 min after the termination of CPB (Table 1).

## Discussion

As the first step in this study, the coronary flow pattern, intracardiac pressure and MvO<sub>2</sub> during aortic cross-clamping were evaluated at several systolic aortic root pressures to determine the systolic aortic root pressure that would maintain coronary flow and heartbeat without cardiac overload during aortic cross-clamping. Next, cardiac function and troponin T before initiation and 120 min after termination of CPB were examined to validate that this systolic aortic root pressure as determined would maintain coronary flow without deterioration of ventricular function during aortic cross-clamping.

Several studies with pig or canine hearts have shown that coronary flow mainly distributes to the epicardial layers because high intramyocardial pressure limits coronary flow to the endocardial layers through a vascular sluice mechanism during systole [7, 11–13]. Intramyocardial pressure is lower during diastole; therefore, diastolic coronary flow is important to prevent endocardial ischemia. In the preliminary study, the diastolic coronary flow ratio during aortic cross-clamping was less than 50% at every systolic aortic root pressure. However, the diastolic coronary flow reached a level comparable to that of the control when the systolic aortic root pressure was maintained above 80 mmHg, with the diminished retrograde coronary flow observed at 60 mmHg of systolic aortic root pressure (Fig. 3B, 5). These phenomena seemed to occur because the diastolic aortic root pressure became elevated along with the systolic aor-

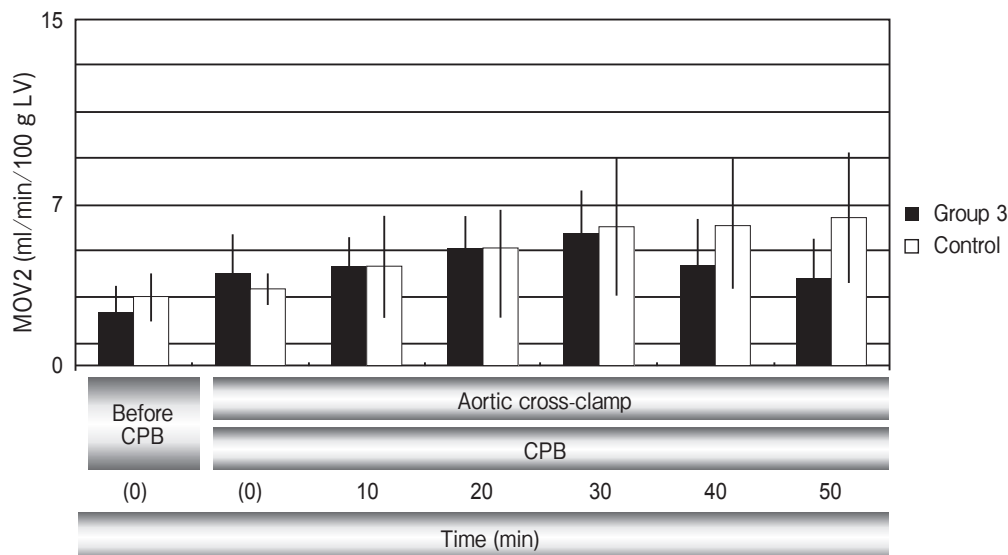


Fig. 4 MvO<sub>2</sub> in study 2. CPB, cardiopulmonary bypass; MvO<sub>2</sub>, myocardial O<sub>2</sub> consumption.

Table 1 Perioperative data in study 2.

	before initiation of CPB			120-minute after CPB		
	Control	group 3	P value	Control	group 3	P value
+dp	1,168 ± 317	1,097 ± 327	NS	1,072 ± 233	1,009 ± 374	NS
−dp	−857 ± 153	−776 ± 123	NS	−704 ± 96	−820 ± 297	NS
Cardiac output (L/min)	1.75 ± 0.16	1.54 ± 0.24	NS	1.7 ± 0.25	1.52 ± 0.25	NS
LV ejection fraction (%)	67.8 ± 9.3	66.8 ± 7.7	NS	62.5 ± 5.9	63.8 ± 5.8	NS
Troponin T (ng/ml)	0.18 ± 0.1	0.14 ± 0.1	NS	0.35 ± 0.13	0.35 ± 0.21	NS

LV, Left ventricular; CPB, cardiopulmonary bypass.



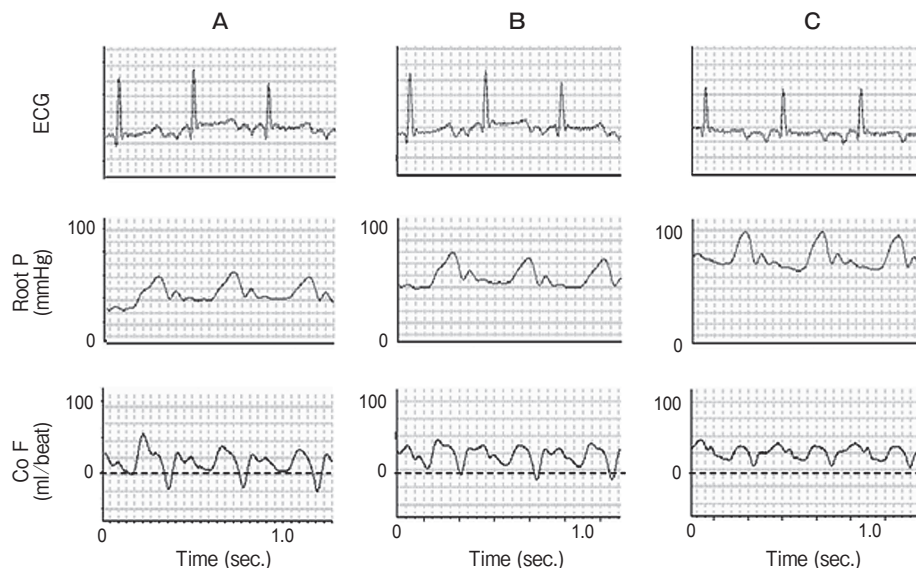


Fig. 5 Actual tracings at systolic aortic root pressure of (A) 60mmHg; (B) 80mmHg; (C) 100mmHg during aortic cross-clamp. Root P, Root pressure; Co F, Coronary flow.

tic root pressure.

An elevated systolic aortic root pressure that leads to increased coronary flow during aortic cross-clamping occurs because of an increase in ventricular preload. Therefore, excessively high systolic aortic root pressures could develop into myocardial failure because of the cardiac overload. In the preliminary study, CVP, LAP and MvO<sub>2</sub> were significantly higher than those of the control group, and LVEDP rose above 9mmHg when the systolic aortic root pressure was above 100mmHg during aortic cross-clamping. Based on these results, 90mmHg of systolic aortic root pressure seemed appropriate to keep the heart beating with an acceptable cardiac preload during aortic cross-clamping.

In study 2, when systolic aortic root pressure was maintained at 90mmHg during 60min of aortic cross-clamping, there was no bradycardia or ST change on an electrocardiogram, and the cardiac function did not deteriorate at all. This result suggests that 90mmHg was the systolic aortic root pressure adequate for maintaining coronary flow during aortic cross-clamping without any affect on cardiac function.

In this experiment, pigs weighing 20kg with normal hearts were used. The use of an animal model in place of human subjects was of course an inherent limitation; although extremely valuable information

was gained, further study will be required before these results can be applied to immature babies with cyanotic heart disease.

In conclusion, maintaining an optimal systolic aortic root pressure maintains the coronary flow and heartbeat without deterioration of cardiac function during 60min of aortic cross-clamping. The results of our study provide a possible approach for aortic arch repair on a beating heart.

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